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Stent placement provides safe esophageal closure in thoracic NOTES™ procedures

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Abstract

Background—Safe esophageal closure remains a challenge in transesophageal Natural Orifice Transluminal Endoscopic Surgery (NOTES). Previously described methods, such as suturing devices, clips, or submucosal tunneling, all have weaknesses. In this survival animal series, we demonstrate safe esophageal closure with a prototype retrievable, antimigration stent.

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Methods—Nine Yorkshire swine underwent thoracic NOTES procedures. A double-channel gastroscope equipped with a mucosectomy device was used to create an esophageal mucosal defect. A 5-cm submucosal tunnel was created and the muscular esophageal wall was incised with a needle-knife. Mediastinoscopy and thoracoscopy were performed in all swine; lymphadenectomy was performed in seven swine. A prototype small intestinal submucosal (SurgiSIS) covered stent was deployed over the mucosectomy site and tunnel. Three versions of the prototype stent were developed. Preneecropsy endoscopy confirmed stent location and permitted stent retrieval. Explanted esophagi were sent to pathology.

Results—Esophageal stenting was successful in all animals. Stent placement took 15.8 ± 4.8 minutes and no stent migration occurred. Preneecropsy endoscopy revealed proximal ingrowth of esophageal mucosa and erosion with Stent A. Mucosal inflammation and erosion was observed proximally with Stent B. No esophageal erosion or pressure damage from proximal radial forces was seen with Stent C. On necropsy, swine 5 had a 0.5-cm periesophageal abscess. Histology revealed a localized inflammatory lesion at the esophageal exit site in swine 1, 3, and 9. The mucosectomy site was partially healed in three swine and poorly healed in six. All swine thrived clinically, except for a brief period of mild lethargy in swine 9 who improved with short-term antibiotic therapy. The submucosal tunnels were completely healed and no esophageal bleeding or stricture formation was observed. All swine survived 13.8 ± 0.4 days and gained weight in the postoperative period.

Conclusions—Esophageal stenting provides safe closure for NOTES thoracic procedures but may impede healing of the mucosectomy site.

Keywords

NOTES; Natural orifice surgery; Transesophageal; Endoscopic; Thoracic; Esophageal stent

Safe esophageal closure remains a challenge in transesophageal Natural Orifice Transluminal Endoscopic Surgery (NOTES) procedures. To date, limited animal studies report transesophageal approaches to mediastinoscopy, thoracoscopy, pleural biopsy, sympathectomy, and mediastinal lymphadenectomy [1–7]. Closure methods include the use of suturing or t-tag devices, which are time-consuming and risk organ injury due to their blind deployment [2]. Endoclips are difficult to deploy in the narrow esophagus and do not provide full-thickness closure of the muscular esophageal wall [1, 2]. Submucosal tunneling techniques, while promising, do not necessarily prevent leakage of esophageal contents into the mediastinum or thorax [1, 5].

Reports have shown that endoluminal esophageal stent placement can be an effective method for the treatment of nonmalignant perforations of the esophagus [8–12]. Retrieval and antimigration are important characteristics of all stents. Additionally, covered stents prevent tissue ingrowth and minimize the proliferation of inflammatory tissue, which facilitates removal [13]. Nonrandomized human studies of stent placement for esophageal leaks and perforations demonstrate rapid leak occlusion, prevention of mediastinal and thoracic contamination, and implementation of earlier nutrition [10, 13].

Based on these encouraging study outcomes, we hypothesized that the use of a submucosal tunnel in conjunction with a retrievable, antimigration stent would achieve a secure esophageal closure after transesophageal NOTES procedures and a good clinical result. To our knowledge, this animal survival series represents the first report of esophageal stent placement after transesophageal NOTES procedures.

Material and methods

This survival study was approved by the Subcommittee for Research Animal Care at the Massachusetts General Hospital, Boston, Massachusetts. The goal of the study was to determine the safety and clinical outcomes of animals undergoing esophageal closure with a prototype small intestinal submucosal (SurgisIS) covered stent. Nine Yorkshire swine underwent thoracic NOTES procedures and then survived for 2 weeks. The animals underwent general anesthesia with induction by Telazol/Xylazine 4.4 mg/kg IM + 2.2 mg/kg IM and endotracheal intubation. Anesthesia was maintained with isoflurane (1.5–3.0%) and oxygen (3.0 l/min.).

In the supine position, a double-channel gastroscope (Pentax Medical Inc., Montvale, NJ) was introduced into the esophageal lumen and used to direct the placement of an overtube in the proximal esophagus. A Duette Multiband mucosectomy device (Cook Medical Inc., Winston-Salem, NC) was fitted on the gastroscope and positioned 10 cm proximal to the gastroesophageal junction. An esophageal mucosal defect was created by aspirating the esophageal mucosa and resecting the banded tissue with an electrocautery snare. A short 5-cm submucosal tunnel was created with both air insufflation and blunt dissection with closed biopsy forceps. A prototype hook knife (Ethicon Endo-Surgery, Cincinnati, OH or Cook Medical Inc.) was used to make an incision through the muscular layers of the esophagus and to enter the mediastinum. Flexible endoscopic scissors (Ethicon Endo-Surgery) or hook knife were used to incise the pleura and permit entry of the endoscope into the thorax. Mediastinoscopy and thoracoscopy were performed in all animals to identify lymph node stations. Lymphadenectomy was attempted in all swine.

A prototype SurgisIS covered metallic stent (Cook Medical Inc.) was deployed over the mucosectomy site and tunnel. Three versions of the prototype stent (Stent A, B, C) were developed (Table 1). Each stent possessed a proximal flare and tiny, circumferential barbs to serve as antimigration properties. To place the stent, a guidewire was first inserted into the esophagus and advanced until it coiled within the stomach. Next, the stent device was placed over the guidewire, and under direct endoscopic visualization, the stent was advanced to the NOTES surgical site. The stent was subsequently deployed over the mucosectomy site and tunnel. If necessary, a loop of string around the proximal cage of the stent allowed the operator to position the stent more proximally after deployment. The stent sheath was removed and the placement reconfirmed with direct visualization.

Postoperatively, there were no dietary restrictions. The swine were monitored for weight gain, ambulation, oral intake, and interactive appearance. Necropsy was performed after 2 weeks. The survival period was determined based on observational results from our previous transesophageal study demonstrating complete mucosal healing in 2-week survival animals [1]. Prenecropsy endoscopy was performed to assess stent location and to attempt stent retrieval. Each animal was examined for any signs of infection, such as thoracic or mediastinal abscess. The esophagi were then explanted and sent for histopathologic review.

Results

Nine animals underwent thoracic NOTES procedures. The right chest was selectively entered in six swine and one node was removed from each animal. The left chest was entered in three swine, but only one animal had a node removed; the remaining swine had no endoscopically visible nodes. Mild-moderate bleeding of a vessel near the lymphadenectomy site occurred in swine 7, requiring placement of two clips to achieve hemostasis. There were no other intraoperative complications.

Esophageal stenting was successful in all animals. Stent placement took 15.8 ± 4.8 minutes and no stent migration occurred. Prenecropsy endoscopy of swine 1–5 revealed severe erosion and ingrowth of esophageal mucosa at the proximal portion of Stent A that precluded retrieval (Fig. 1). Although improved, mucosal inflammation and erosion was again observed at the proximal portion of Stent B used in swine 6 and 7 (Fig. 2). No proximal esophageal erosion or pressure damage was seen in the swine that received Stent C. Stents B and C were retrieved before necropsy. No esophageal bleeding or stricture formation was observed in any swine.

On necropsy, the mediastinum and thorax were thoroughly evaluated (Table 2). There was no evidence of injury to mediastinal or thoracic structures. Swine 5 had a small, 0.5-cm periesophageal abscess. Fibrinous material and adhesions were seen in swine 7 as a result of the intrathoracic bleeding. Four swine had no pleural fluid in the thoracic cavity and five had a small amount. No evidence of free esophageal perforation or gross signs of mediastinitis or lung empyema was seen in any of the animals.

In all animals, the submucosal tunnel was well healed, whereas the transesophageal exit sites showed transmural fibrosis and in some cases chronic inflammation. In swine 1, 3, and 9, histology revealed a localized fluid collection at the esophageal exit site consisting of acute inflammatory cells in the esophageal wall. Gram stain on each of these collections showed no organisms. The mucosectomy site was partially healed (granulation tissue not surfaced by squamous epithelium, but restituted, regenerative squamous epithelium seen at periphery) in three swine and poorly healed (granulation tissue involving the wall, including submucosa and muscularis propria, without restitution of the squamous epithelium overlying it) in six swine (Table 2). Figure 3 shows partial healing of the esophageal mucosectomy site.

All swine thrived clinically except a brief period of mild lethargy in swine 9 on postoperative day 3. This animal improved with short-term antibiotic therapy. The nine swine were survived for 13.8 ± 0.4 days. Eight animals gained weight during the postoperative period; weight was not recorded in swine 1.

Discussion

This study is the first report of secure esophageal closure in NOTES thoracic procedures using a prototype esophageal stent. In previous studies, esophageal closure methods included clips, suturing devices, and the submucosal tunneling technique alone [1, 2, 5, 6]. Clips often are difficult to deploy in the narrow esophagus and result in superficial closure with discontinuation of the esophageal muscular layers on histology [2]. Prototype suturing devices are more likely to result in full-thickness healing [2] but can be cumbersome, time-consuming, and require the blind placement of T-tag anchors, which risk damage to surrounding structures. The submucosal tunneling technique creates a flap-valve that offsets the proximal mucosal incision from the distal incision through the esophageal muscle layers. Upon withdrawal of the endoscope, the tunnel collapses. This technique has served as sufficient closure in many studies [1, 5]. Nevertheless, there is always a concern that esophageal contents may travel through the tunnel and contaminate the mediastinum and thorax during the early postoperative period. In this study, we investigated the use of an esophageal stent as an adjunct to the mucosal flap-valve.

Numerous reports in the thoracic surgery literature have demonstrated the effectiveness of an esophageal stent for nonmalignant perforations of the esophagus [8–14]. Key characteristics of such a stent include retrievability and antimigration design. This concept is comparable to transesophageal NOTES thoracic procedures where an incision is purposefully made through the esophagus to access the mediastinum and thorax.

Three different versions of a prototype esophageal stent were used. Each stent had a proximal flare with tiny barbs designed to prevent migration. The uncovered proximal flare in Stent A led to ingrowth of esophageal mucosa and precluded retrieval. Subsequently, the proximal flare of Stent B was covered with plastic to prohibit tissue ingrowth and make stent retrieval possible. Mucosal inflammation and erosion persisted upon stent removal and may have resulted from high radial forces, the circumferential barbs on the stent, or both. The overall stent diameter and length was decreased in Stent C. There was no migration and the stent remained retrievable. More importantly, there was no visible mucosal irritation or inflammation surrounding the proximal portion of the stent on preneecropsy endoscopy. This result is likely from decreased radial forces to the esophageal wall.

The prototype stent also was created to assess the potential value of a SurgiSIS covering in promoting healing at the mucosectomy site. We hypothesized that this may facilitate healing, because SurgiSIS mesh has been successfully used in hernia repair in humans with good results [15–17]. In the current study, a SurgiSIS covering did not appear to augment healing of the mucosectomy, but no definitive conclusions regarding the efficacy of SurgiSIS can be drawn in this trial. A study directly comparing the use of a BioMesh covered stent to a standard covered stent would be necessary to help eliminate the mere presence of a stent as the cause for delayed healing.

In six of the animals there was incomplete healing of the mucosal defect, and in three of the animals partial healing was present. The submucosal tunnel, however, was completely healed in all animals. This result raises the interesting question of whether tissue ischemia induced by the radial force of the stent could have been responsible for the impaired healing of the mucosectomy site. Our previous transesophageal NOTES survival studies [1] resulted in evidence of better healing of the mucosectomy site after 2-week survival; however, one animal in the study developed a fluid collection and subsequent abscess in the submucosal tunnel. Diversion of the intraluminal esophageal contents could have prevented such an outcome.

Infectious complications are always a concern with NOTES surgical procedures. On gross examination, one animal (swine 5) had a 0.5-cm periesophageal abscess. Three other animals (swine 1, 3, 9) had localized fluid collections at the esophageal exit site containing acute inflammatory cells that were sterile on gram stain. These sterile fluid collections likely represent the normal postoperative healing process. All of the animals thrived in the postoperative period, except one with mild lethargy that was responsive to 3 days of antibiotic therapy. The animals did not receive standard postoperative antibiotics as part of our protocol, although its implementation could have prevented the postoperative infectious complication.

Limitations to this study include the small sample size and short-term survival. A longer survival period may have demonstrated improved healing of the mucosal defect regardless of stenting, but the healing time would likely still be inferior to the use of submucosal tunneling alone. In addition, the role of SurgiSIS in mucosal healing is unclear and requires direct comparison to animals receiving the same stent with a conventional covering alone. Finally, future studies are needed in larger numbers of animals to assess whether esophageal stenting, submucosal tunneling, clips, or endoscopic sutures produce the best clinical outcome and afford the most rapid healing of the surgical site.

In this study, esophageal stent placement successfully diverted intraluminal contents from the tunnel, thus preventing contamination of the mediastinum and thorax and allowing animals to resume their oral intake in the immediate postoperative period. Although the esophageal mucosal defects did not completely heal during the 2-week survival period, the

submucosal tunnels healed well. Based on our data, the submucosal tunneling technique combined with esophageal stent placement is a safe and effective method of esophageal closure in thoracic NOTES procedures.

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Fig. 1.
Stent A: erosion and ingrowth of esophageal mucosa at the proximal cage of the stent. The SurgiSIS material covering the stent is partially degraded revealing the underlying plastic

Fig. 2.
Stent B: proximal mucosal erosion and inflammation

Fig. 3. Partial healing of a mucosectomy site is seen here as an ovoid defect in the mucosa. The proximal portion of the esophagus (right side of image) demonstrates tissue ingrowth at proximal portion of the stent

Table 1

Prototype stent specifications

Stent	Swine no.	Diameter proximal cage (mm)	Diameter (body) (mm)	Stent length (mm)	Plastic covered proximal cage	Surgisis/plastic covered body cage	Plastic covered distal cage
A	1–5	45	28	80	No	Yes	Yes
B	6–7	45	28	80	Yes	Yes	Yes
C	8–9	37	22	65	Yes	Yes	Yes

Table 2

Necropsy findings

Swine no.	Pleural fluid	Fluid collection on necropsy	Fluid collection on pathology	Mucosectomy site (partial ^a vs. poor ^b healing)
1	None	No	Yes ^c (exit site)	Partial
2	Small	No	No	Poor
3	Small	No	Yes ^c (exit site)	Poor
4	None	No	No	Poor
5	Small	Yes (periesophageal)	No	Partial
6	Small	No	No	Poor
7	None	No	No	Partial
8	None	No	No	Poor
9	Small	No	Yes ^c (exit site)	Poor

^a Partial healing: center of granulation tissue not surfaced by squamous epithelium, but restituted, regenerative squamous epithelium seen at periphery

^b Incomplete healing: granulation tissue involving the wall (including submucosa and muscularis propria) without restitution of the squamous epithelium overlying it

^c No organisms seen on gram stain